

### REMARKS

It is respectfully requested that this application be reconsidered in view of the above amendments and the following remarks and that all of the claims remaining be allowed.

#### Claim Amendments

Although it is clear that a cellular composition for transplantation into a recipient must be *ex vivo*, claims 18 and 19 have been amended to recite "*ex vivo*" for additional clarity. Support for this recitation can be found throughout the application, for instance, in Examples 1-4, where all cellular compositions were treated with reoviruses *ex vivo*.

Claim 19 has also been amended to adopt a more clear style, by changing "further comprising the step of" to step (c).

New claims 38-49 have been added. Support for claims 38-42 and 44-48 can be found, for example, in the original claims 2-6. Support for claim 43 and 49 can be found, for example, in the original claim 8.

No new matter has been added by these amendments. The Examiner is hereby requested to enter these amendments.

Applicants submit that all claim amendments presented herein or previously are made solely in the interest of expediting allowance of the claims and should not be interpreted as acquiescence to any rejections or ground of unpatentability. Applicants reserve the right to file at least one continuing application to pursue any subject matter that is canceled or removed from prosecution due to the amendments.

### Interview

Applicants wish to thank Examiner Harris for extending the courtesy of discussing the application with the undersigned and making helpful suggestions on November 21, 2003. As this amendment and reply is prepared pursuant to these discussions and suggestions, Applicants submit that all pending claims are in condition for allowance.

### Rejection Under 35 U.S.C. §103

#### A. Coffey et al. and Freshney (Paragraph 8 of the Office Action)

The rejection of claims 18, 25, 27-31 and 37 under 35 U.S.C. §103(a) over Coffey et al. (Science 282:1332-1334, 1998) and in view of Freshney (Culture of Animal Cells: A Manual of Basic Technique, 2<sup>nd</sup> Ed., New York, NY, 1987), is respectfully traversed for the reasons set forth below.

To properly issue a rejection under 35 U.S.C. §103, the USPTO bears the initial burden to establish a prima facie case of obviousness by meeting three criteria. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings to arrive at the claimed invention. *In re Vaeck*, 20 USPQ 2d 1438 (Fed. Cir. 1991). Second, there must be a reasonable expectation of success. *Id.* Finally, the prior art reference or the combination of references must teach or suggest all the claim limitations. *In re Royka*, 180 USPQ 580 (CCPA 1974).

These criteria are not met in the instant rejection. Claim 18 recites a method of preparing a cellular composition for transplantation into a recipient, comprising the steps of:

- (a) selecting a cellular composition for transplantation; and
- (b) contacting the composition with a reovirus to result in oncolysis of ras-mediated neoplastic cells;

wherein said transplantation is autologous.

Similarly, claim 19 is directed to a method of preparing a cellular composition for transplantation into a recipient, comprising the steps of:

- (a) selecting a cellular composition for transplantation;
- (b) contacting the composition with a reovirus to result in oncolysis of ras-mediated neoplastic cells; and
- (c) administering to the transplant recipient at least one substance selected from the group consisting of anti-reovirus antibodies and immune system stimulating agents.

All other rejected claims depend ultimately from claim 18 or 19, thereby reciting all the elements of claim 18 or 19, respectively.

Coffey et al. teach the use of reovirus in the oncolysis of ras-transformed cells. It was also disclosed in Coffey et al. that when ras-mediated cells were implanted in syngeneic mice to form tumors, administration of reoviruses to the tumor-bearing mice resulted in tumor regression. However, Coffey et al. do not teach or suggest treating any cellular composition with reovirus outside of a living organism for the purpose of transplanting the treated composition into an animal.

The Office Action, in regard to Coffey et al., states that "it would have been prima facie obvious .... to prepare a cellular composition contacted with a oncolytic reovirus for autologous transplantation because clearly the syngeneic transplantation was effective in tumor regression and increased morbidity" (page 4, last paragraph of the Office Action; emphasis added).

Applicants wish to point out that Coffey et al. implanted transformed C3H-10T1/2 cells into syngeneic animals to form tumors. After the tumors had established, the animals were used as a tumor model to test the effects of treatments (see page 1333, middle column of Coffey et al.) Therefore, the syngeneic transplantation in Coffey et al. was performed to form tumors, and it did not result in tumor regression or increased morbidity. Nowhere do Coffey et al. teach or suggest transplanting a reovirus-treated cellular composition into an animal.

Freshney teaches a method for freezing animal cell lines by suspending the cells in culture medium containing a preservative, and freezing the resultant mixture at a low temperature. Freshney does not teach or suggest treating any cellular composition with reovirus outside of a living organism for the purpose of transplanting the treated composition into an animal.

Taken together, the two references do not teach or suggest all the elements of the claimed invention, particularly the treatment of a cellular composition with reovirus outside of a living organism for the purpose of transplanting the treated composition into an animal. Nor does the combination of references provide any motivation to modify the combined teachings to arrive at the claimed invention, or a reasonable expectation of success. Therefore, the requirement under 35 U.S.C. §103 is not met.

Accordingly, withdrawal of this rejection is respectfully requested.

**B. Coffey et al. and U.S. Patent Number 6,136,307 (Paragraph 9 of the Office Action)**

The rejection of claims 18, 25-29 and 31 under 35 U.S.C. §103(a) over Coffey et al. (Science 282:1332-1334, 1998) and in view of U.S. Patent Number 6,136,307, is respectfully traversed for the same reasons set forth above. Briefly, as described above, Coffey et al. do not teach or suggest treating any cellular composition with reovirus outside of a living organism for the purpose of transplanting the treated composition into an animal. U.S. Patent Number 6,136,307 teaches the administration of reoviruses to an animal in order to treat ras-mediated proliferative disorders. However, it does not specifically teach or suggest treating any cellular composition with reovirus outside of a living organism for the purpose of transplanting the treated composition into an animal.

Thus, neither cited reference teaches or suggests all the requirement element of the claimed invention, and combining the references does not cure the deficiency. In addition, the combination of references does not provide any motivation to modify the combined teachings to arrive at the claimed invention. Therefore, the requirement under 35 U.S.C. §103 is not met.

Accordingly, withdrawal of this rejection is respectfully requested.

C. Coffey et al., U.S. Patent Number 5,861,159, Freshney, and U.S. Patent Number 6,136,307 (Paragraph 10 of the Office Action)

Similarly, the rejection of claims 18, 19 and 25-37 under 35 U.S.C. §103(a) over Coffey et al. (Science 282:1332-1334, 1998) and in view of U.S. Patent Number 5,861,159, Freshney (Culture of Animal Cells: A Manual of Basic Technique, 2nd Ed., New York, NY, 1987), and U.S. Patent Number 6,136,307, is respectfully traversed for the reasons set forth below.

As described above, none of Coffey et al., Freshney, and U.S. Patent Number 6,136,307 teaches or suggests treating a cellular composition with reovirus outside of a living organism for the purpose of transplanting the treated composition into an animal. U.S. Patent Number 5,861,159 teaches controlled release of immunopotentiating agents, but not the use of reovirus to treat a cellular composition outside of a living organism for the purpose of transplanting the treated composition into an animal. Consequently, the four cited references, either alone or in any combination thereof, do not teach or suggest all the elements of the claimed invention. Nor do the references provide any motivation to modify the combined teachings to arrive at the claimed invention.

Accordingly, the requirement under 35 U.S.C. §103 is not met, and withdrawal of this rejection is respectfully requested.

Applicant : Morris, et al.  
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Conclusions

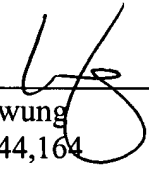
For the reasons set forth above, Applicants submit that the claims of this application are patentable. Reconsideration and withdrawal of the Examiner's rejections are hereby requested. Allowance of the claims remaining in this application is earnestly solicited.

In the event that a telephone conversation could expedite the prosecution of this application, the Examiner is requested to call the undersigned at (650) 839-5044.

Enclosed is a \$27.00 check for excess claim fees. Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

Date: Dec. 23, 2003

  
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